REMARKS

Examination of claims 5-12, 14-18, 25, and 37-46 is reported in the final Office Action. Claims 5-10, 14-18, 25, 37-42, 45, and 46 were rejected under 35 U.S.C. § 112, first paragraph (scope); claims 5, 10, 25, and 42 were rejected under 35 U.S.C. § 112, first paragraph (written description); Claims 5-9, 16, 17, 34, 37, 38, 42, and 44 were rejected under 35 U.S.C. § 112, second paragraph; Claims 5, 6, 10-12, 14-16, 18, 25, 37, and 39-44 were rejected under 35 U.S.C. § 102(b); claims 5, 17, 25, 38, and 45 were rejected under 35 U.S.C. § 103(a). Each of the rejections is addressed as follows.

First, applicants note that in an Advisory Action dated March 25, 2003, it is stated that the After Final Amendment that was filed in this case on March 5, 2003 was not entered, because the proposed amendment to claim 7 would broaden the scope of claim 5, from which claim 7 indirectly depends, thus raising a new issue. In particular, the amendment to claim 7 proposed in the March 5, 2003 submission includes the words "further comprising," which the Examiner notes opens the scope of claim 5, which includes the words "consisting essentially of." The proposed amendment to claim 7 was not intended to allow the inclusion of additional steps in the method of claim 5, but rather was intended to show that the induced immune response also included a Th2 immune response. To clarify this matter, claim 7 has been amended to remove the language "further comprising."

Rejection under 35 U.S.C. § 112, first paragraph (enablement and written description)

Claims 5-10, 14-18, 25, 37-42, 45, and 46 were rejected under § 112, first paragraph for lack of enablement (scope), with the Examiner stating that the specification does not enable the administration of any *Helicobacter pylori* peptide or polypeptide, or any DNA molecule or

vaccinal vector encoding such a peptide or polypeptide, for the purpose of preventing or treating Helicobacter infection. The Examiner further states that although the previously submitted declarative evidence partially overcame this rejection, it is not commensurate in scope with the invention as claimed, apparently because the claims include within their scope DNA molecules encoding *H. pylori* polypeptides, *H. pylori* peptides, and therapeutic treatment of *H. pylori* infection. In the interest of expediting prosecution, the claims have been amended to specify that which the Examiner has deemed to be enabled: the use of prophylactically effective *H. pylori* polypeptide antigens in methods of inducing a prophylactic immune response, using the specific regimens and routes specified in the claims. Applicants thus respectfully request that this rejection be withdrawn. Applicants further note that they reserve the right to pursue the previous or similar claims in future, continuation applications.

Claims 5, 10, 25, and 42 were also rejected under § 112, first paragraph on the basis that these claims include subject matter that was not described in the specification in such a way so as to convey to those of skill in this art that the applicants were in possession of the claimed invention at the time the application was filed. This rejection is based upon the inclusion in applicants' claims of references to DNA molecules encoding Helicobacter antigens. As is noted above, in the interest of expediting prosecution, claims specifying use of DNA molecules have been canceled, without prejudice. The claimed methods now specify the use of prophylactically effective polypeptide antigens of *H. pylori*. Applicants thus respectfully request that this rejection be withdrawn.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 5-9, 16, 17, 34, 37, 38, 42, and 44 were rejected under 35 U.S.C. § 112, second paragraph on several grounds, which are addressed as follows.

The previous rejection of claims 7-9 under § 112, second paragraph as being indefinite has been maintained. This rejection is based on the fact that one type of immune response is recited in the preambles of these claims, while in the body of these claims, more than one type of immune response is noted. As was noted in their previous reply, applicants disagree with this rejection, as the second type of immune response indicated in the bodies of these claims is recited only as a frame of reference in which the type of immune response recited in the claims preambles can be further characterized. Regardless, in the interest of expediting prosecution, these claims have been amended so that the preambles of these claims no longer specify the type of immune response being induced. Rather, the preambles state that an immune response is induced, and the details as to the types of immune responses induced are present in the bodies of these claims. Applicants thus respectfully request that this rejection be withdrawn.

Claim 5 was rejected for including the term "effective," on the basis that it is not clear what the amount is effective for. This rejection has been met by the present amendment to claim 5, which now states that a prophylactically effective amount of a prophylactically effective *H. pylori* antigen is employed in the method.

Claims 5 and 6 were rejected for including the phrase "subdiaphragmatic, systemic route," on the basis that the terms in this phrase are inconsistent with one another. In particular, the Examiner notes that the "subdiaphragmatic" region of the body is limited to the part of a mammal below the diaphragm, while the term "systemic" would include administration to areas that are above the diaphragm. Applicants respectfully request that this rejection be withdrawn.

It is clear that what is meant by the "subdiaphragmatic, systemic" route is administration in a non-mucosal manner in the part of the body below the diaphragm. This is supported, for example, on page 6, throughout which the terms systemic and parenteral are used together. In addition, on page 6, line 28 - page 7, line 1, it is clearly stated that "the administration by the systemic or parenteral route is advantageously carried out in the subdiaphragmatic part of the mammal." This interpretation of the phrase "subdiaphragmatic, systemic" is also supported in the Examples of the application, which demonstrate administration by such methods.

Claims 16 and 17 have been canceled without prejudice and, thus, the rejection of these claims under § 112, second paragraph is moot.

Claim 34 was rejected in reciting the phrase "in which a ... is co-adminstered," with the Examiner suggesting that applicants amend this claim to recite an active step, rather than using the passive voice. This rejection has been addressed in the manner suggested by the Examiner and, thus, applicants respectfully request that the rejection be withdrawn.

Claims 37 and 38 were rejected for reciting steps in addition to those recited in claim 25, from which claims 37 and 38 depend. The Examiner states that these claims broaden the scope of claim 25, which specifies a particular order of mucosal and parenteral administration steps. Applicants respectfully disagree with this rejection. In particular, claims 37 and 38 do not negate the requirement for a mucosal step followed by a parenteral step, as is specified in claim 25. Rather, these claims add additional steps to the ordered steps of claim 25. To clarify what was intended by these claims, they have each been amended to specify that they are drawn to the method of claim 25 further comprising an additional mucosal (claim 37) or parenteral (claim 38) step. The original mucosal and parenteral steps of claim 25 are not changed by the addition of these steps.

Claims 42 and 44 have been canceled without prejudice and, thus, the rejection of these claims under § 112, second paragraph is moot.

The Examiner notes that the use of the trademarks QS-21, DC-Chol, and Bay should be capitalized and accompanied by generic terminology. The specification has been amended accordingly.

Rejections under 35 U.S.C. § 102(b)

Claims 5, 10, 11, 14, and 15 were rejected under 35 U.S.C. § 102(b) as being anticipated by Lee et al. (1995), on the basis that this reference teaches a method of inducing an immune response to an *H. pylori* composition administered subcutaneously. Applicants respectfully request that this rejection be withdrawn because, as is discussed above, the present claims require that administration take place beneath the level of the diaphragm, and such administration is not mentioned in the Lee reference.

Claims 5, 10, 14, and 15 were also rejected under § 102(b) as being anticipated by Laszlo et al. (1992), on the basis that this reference also teaches a method of inducing an immune response to an *H. pylori* composition administered subcutaneously. Applicants respectfully request that this rejection be withdrawn because, as is discussed above, the present claims require that administration take place beneath the level of the diaphragm, and such administration is not mentioned in the Laszlo reference.

Claims 5, 6, 10, 12, 14-16, 18, 25, 37, and 39-44 were rejected under § 102(b) as being anticipated by WO 96/31235, in light of U.S. Patent No. 6,126,938. This rejection is based on the assertion that the cited reference teaches the administration of an antigen to the dorsolumbar region, which the Examiner states is subdiaphragmatic.

Applicants respectfully request that this rejection be withdrawn. In particular, applicants note that claim 5, from which claims 6, 10, 12, 14-16, and 18 depend, has been amended to specify that the method consists essentially of subdiaphragmatic, systemic administration, thus excluding the use of additional administration routes in the method. The cited reference describes the use of dorsolumbar administration in the context of a method requiring also nasal and/or buccal administration (column 4, lines 60-65) and administration by an additional mucosal route (column 4, line 66 - column 5, line 7). Thus, the cited reference does not describe the invention of claims 5, 6, 10, 12, 14-16, and 18, and the rejection should be withdrawn with respect to these claims.

This rejection should also be withdrawn with respect to claims 25, 37, and 39-44, as these claims require administration by a mucosal route, followed by a parenteral route, and the cited reference nowhere describes such a method. Rather, the passage referred to in the Office Action as supporting this rejection (column 7, lines 44-50) simply specifies that administration by the nasobuccal route is combined with systemic administration, but does not specify the particular order required by the present claims. Applicants also note that claim 40 requires that the mucosal administration step of claim 25 be oral, and the reference certainly does not mention administration by such a route, followed by parenteral administration. Applicants thus respectfully request that this rejection be withdrawn.

Rejection under 35 U.S.C. § 103(a)

Claims 5, 17, 25, 38, and 45 were rejected under § 103(a) for obviousness over Guy et al., WO 96/31235, which is in the French language, in light of Guy et al., U.S. Patent No. 6,126,938,

the English language specification of which corresponds to that of WO 96/31235, in view of Thomas, Jr. et al. (U.S. Patent No. 5,919,463). This rejection is respectfully traversed.

The Examiner states that the Guy reference differs from the rejected claims by failing to show the combination of an *H. pylori* antigen and a *C. difficile* adjuvant. Applicants respectfully disagree. As is discussed above, claim 5 (and thus dependent claim 17) specifies a method that consists essentially of subdiaphragmatic, systemic administration, and the Guy reference does not describe or provide motivation to carry out such a method. Rather, the methods described in the Guy reference require the use of at least two routes of administration and provides no basis to believe that use of only one route, and in particular that specified by these claims, would be effective. The Thomas reference also does not provide such a suggestion or motivation. Rather, the main focus of the Thomas reference is the use of *C. difficile* toxins as mucosal adjuvants, and the reference provides no motivation or suggestion to use such toxins as adjuvants in subdiaphragmatic administration methods such as those now claimed.

This rejection should also be withdrawn with respect to claim 25 (and dependent claims 38 and 45), because, as is discussed above, the Guy reference does not teach the use of a method involving mucosal administration followed by parenteral administration, and does not provide any motivation to carry out such a method. Indeed, the entire focus of the Guy reference is the identification of <u>other</u> effective immunization routes. The Thomas reference also fails to even mention methods involving mucosal followed by parenteral administration. Applicants thus respectfully request that this rejection be withdrawn.

Claims 5, 17, 25, 38, and 45 were also rejected under § 103(a) for obviousness over the Guy reference, in view of Lee (U.S. Patent No. 5,837,240). The Examiner states that the teachings of the Guy reference differ from the present claims by failing to show the combination

of an *H. pylori* antigen with LT or CT adjuvants, and the administration of an *H. pylori* antigen by the parenteral route more than once.

Applicants respectfully disagree with this rejection. As is discussed above, claim 5 (and thus dependent claim 17) specifies a method that consists essentially of subdiaphragmatic, systemic administration, and the Guy reference does not describe or provide motivation to carry out such a method. Rather, the methods described in the Guy reference require the use of at least two routes of administration and provides no basis to believe that use of only one route, and in particular that specified by these claims, would be effective. The Lee reference also does not provide such a suggestion or motivation. Rather, the main focus of the Lee reference is the use CT and LT with as parenteral adjuvants in *H. pylori* immunization methods, and the reference provides no motivation or suggestion to use such toxins as adjuvants in subdiaphragmatic administration methods such as those now claimed.

This rejection should also be withdrawn with respect to claim 25 (and dependent claims 38 and 45), because, as is discussed above, the Guy reference does not teach the use of a method involving mucosal administration followed by parenteral administration, and does not provide any motivation to carry out such a method. Indeed, the entire focus of the Guy reference is the identification of <u>other</u> effective immunization routes. The Lee reference also fails to even mention methods involving mucosal followed by parenteral administration. Applicants thus respectfully request that this rejection be withdrawn.

CONCLUSION

Applicants submit that the claims are in condition for allowance, and such action is respectfully requested. In addition, applicants request that further correspondence in this case be mailed to them at the following address:

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If there are any additional charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: September 5, 2003

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